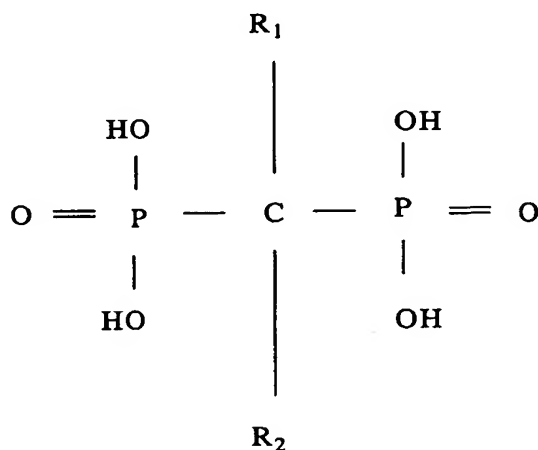


WHAT IS CLAIMED IS:

1. A pharmaceutical composition, comprising a non-activated metabolite of vitamin D₂ and/or D₃, and at least one bisphosphonate.

5

2. The pharmaceutical composition according to Claim 1, wherein the bisphosphonate is of the formula:



wherein R₁ is independently selected from H, OH and Cl, and R₂ is
 10 independently selected CH₃, Cl, CH₂CH₂NH₂, (CH₂)₃NH₂, CH₂-3-pyridine, CH₂-S-phenyl-Cl, CH₂CH₂N(CH₃)(pentyl), CH₂-imidazole, CH₂-2-imidazo-pyridinyl, N-(cycloheptyl), CH₂CH₂N(CH₃)₂, CH₂)₅NH₂, and CH₂-1-pyrrolidinyl, and combinations thereof.

15 3. The pharmaceutical composition according to Claim 2, suitable for preventing or treating abnormal bone resorption, wherein the composition, comprises a pharmaceutically effective amount of at least one bisphosphonate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof is from about 0.05 to about 560 mg, on an alendronic acid active weight basis, and the
 20 supplementary effective amount of non-activated metabolite of vitamin D₂ and/or D₃ is from about 100 to about 60,000 IU.

4. The pharmaceutical composition according to Claim 3, wherein the bisphosphonate is selected from ibandronate, minodronate, pamidronate, risedronate, zoledronate, alendronate and combinations thereof.

5

5. The pharmaceutical composition according to Claim 4, wherein the bisphosphonate is alendronate.

6. The pharmaceutical composition according to Claim 5, suitable for administration at intervals of once-weekly, bi-weekly, monthly, twice-monthly, and bi-monthly.

7. The pharmaceutical composition according to Claim 6, wherein the composition is in a form selected from compressed, coated, or un-coated tablets, capsules, hard or gelatin capsules, pellets, elixirs, syrups, slurries, emulsions, suspensions, solutions, effervescent and effervescent-buffered compositions, powders, and films.

8. A pharmaceutical composition suitable for inhibiting abnormal bone resorption in a mammal, in need thereof, comprising a supplementary effective amount of from about 100 to about 60,000 IU of a non-activated metabolite of vitamin D₂ and/or D₃, and a pharmaceutically effective amount of from about 0.05 to about 560 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis.

9. A method for preventing or treating metabolic bone disease in a mammal, in need thereof, comprising concomitantly, orally administering to said mammal pharmaceutical compositions comprising a supplementary effective amount of a non-activated metabolite of vitamin D₂ and/or D₃, and a pharmaceutically effective amount of at least one bisphosphonate, as unit dosages, according to a continuous dosing schedule, wherein administration is performed, simultaneously or

alternately, according to dosing intervals of once-weekly, twice-weekly, bi-weekly, once-monthly, and bi-monthly.

10. The method for preventing or treating abnormal bone
5 resorption in a mammal according to Claim 9, wherein the supplementary amount of non-activated metabolite of vitamin D₂ and/or D₃ is from about 100 to about 60,000 IU, and the pharmaceutically effective amount of alendronate is from about 0.05 to about 560 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis.

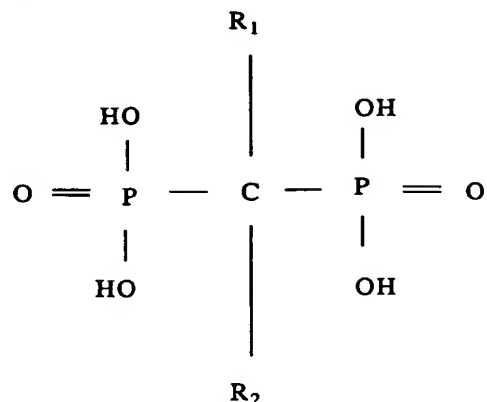
10

11. A method for preventing or treating abnormal bone resorption
in a mammal, in need thereof, comprising orally administering to said mammal a pharmaceutical composition, comprising a supplementary effective amount of a non-activated metabolite of vitamin D₂ and/or D₃, and a pharmaceutically effective amount
15 of at least one bisphosphonate, as a unit dosage according to a continuous administration schedule.

12. The method of treating a disease according to Claim 11,
wherein the disease is selected from osteoporosis, post-menopausal osteoporosis,
20 steroid-induced osteoporosis, male osteoporosis, other disease-induced osteoporosis, idiopathic osteoporosis, and glucocorticoid-induced osteoporosis; Paget's disease; osteoarthritis, abnormally increased bone turnover; localized bone loss associated with periprosthetic bone loss or osteolysis; bone fractures; metastatic bone disease; Gaucher's disease, avascular necrosis, polyostotic fibrous dysplasia, Charcot's joint,
25 parasitic disorders, osteogenesis imperfecta, homocystinuria, lysinuric protein intolerance, Turner's syndrome, immobilization, fibrous dysplasia, fibrogenesis imperfecta ossium, periodontal disease, tooth loss, hypercalcemia of malignancy; multiple myeloma; and osteopenia, immobilization-induced osteopenia and osteopenia due to bone metastases.

30

13. The method according to Claim 12, wherein the bisphosphonate is of the general formula:



wherein R₁ is independently selected from H, OH and Cl, and R₂ is
 5 independently selected CH₃, Cl, CH₂CH₂NH₂, (CH₂)₃NH₂, CH₂-3-pyridine, CH₂-S-phenyl-Cl, CH₂CH₂N(CH₃)(pentyl), CH₂-imidazole, CH₂-2-imidazo-pyridinyl, N-(cycloheptyl), CH₂CH₂N(CH₃)₂, (CH₂)₅NH₂, and CH₂-1-pyrrolidinyl, and combinations thereof.

10 14. The method according to Claim 13, wherein the pharmaceutically effective amount of at least one bisphosphonate is from about 0.05 to about 560 mg, on an alendronic acid active weight basis.

15 15. The method according to Claim 14, wherein the bisphosphonate is selected from ibandronate, minodronate, pamidronate, risedronate, zoledronate, alendronate and combinations thereof.

20 16. The method according to Claim 15, wherein the bisphosphonate is alendronate.

17. The method according to Claim 16, wherein the supplementary effective amount of a non-activated metabolite of vitamin D₂ and/or D₃ is from about 100 to about 60,000 IU.

18. The method according to Claim 17, wherein the dosing interval is selected from once-weekly, twice-weekly, bi-weekly, once-monthly, and bi-monthly.

5

19. The method according to Claim 18, wherein the dosing interval is once-weekly.

20. The method according to Claim 19, wherein the composition is in a form selected from compressed, coated, or un-coated tablets, capsules, hard or gelatin capsules, pellets, elixirs, syrups, slurries, emulsions, suspensions, solutions, effervescent and effervescent-buffered compositions, powders, films, and the like.

21. A method for preventing or treating abnormal bone resorption in a mammal, in need thereof, comprising orally administering to said mammal a pharmaceutical composition comprising a supplementary effective amount of from about 100 to about 60,000 IU of a non-activated metabolite of vitamin D₂ and/or D₃ and a pharmaceutically effective amount of from about 0.05 to about 560 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein the dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

22. A pharmaceutical composition suitable for oral administration for the treatment or prevention of abnormal bone resorption in mammals, in need thereof, comprising a unit dosage of a supplementary effective amount of at least about 2,800 IU of a non-activated metabolite of vitamin D₂ and/or D₃, and a pharmaceutically effective amount of at least about 70 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein the dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

- 30

23. A pharmaceutical composition suitable for oral administration for the treatment or prevention of abnormal bone resorption in mammals, in need thereof, comprising a unit dosage of a supplementary effective amount of at least
5 about 5,600 IU of a non-activated metabolite of vitamin D₂ and/or D₃, and a pharmaceutically effective amount of at least about 70 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein the dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

10

24. A pharmaceutical composition suitable for oral administration for the treatment or prevention of abnormal bone resorption in mammals, in need thereof, comprising a unit dosage of a supplementary effective amount of at least
15 about 2,800 IU of a non-activated metabolite of vitamin D₂ and/or D₃, and a pharmaceutically effective amount of at least about 35 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein the dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

20

25. A pharmaceutical composition suitable for oral administration for the treatment or prevention of abnormal bone resorption in mammals, in need thereof, comprising a unit dosage of a supplementary effective amount of at least
25 about 5,600 IU of a non-activated metabolite of vitamin D₂ and/or D₃, and a pharmaceutically effective amount of at least about 35 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein the dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

26. A method of preventing or treating abnormal bone resorption in
30 a mammal, in need thereof, comprising orally administering to said mammal a

pharmaceutical composition comprising a unit dosage of a supplementary effective amount of at least about 2,800 IU of a non-activated metabolite of vitamin D₂ and/or D₃ and a pharmaceutically effective amount of at least about 70 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

27. A method of preventing or treating abnormal bone resorption in a mammal, in need thereof, comprising orally administering to said mammal a pharmaceutical composition comprising a unit dosage of a supplementary effective amount of at least about 5,600 IU of a non-activated metabolite of vitamin D₂ and/or D₃ and a pharmaceutically effective amount of at least about 70 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein the dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

28. A method of preventing or treating abnormal bone resorption in a mammal, in need thereof, comprising orally administering to said mammal a pharmaceutical composition comprising a unit dosage of a supplementary effective amount of at least about 2,800 IU of a non-activated metabolite of vitamin D₂ and/or D₃ and a pharmaceutically effective amount of at least about 35 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein the dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

29. A method of preventing or treating abnormal bone resorption in a mammal, in need thereof, comprising orally administering to said mammal a pharmaceutical composition comprising a unit dosage of a supplementary effective amount of at least about 5,600 IU of a non-activated metabolite of vitamin D₂ and/or D₃ and a pharmaceutically effective amount of at least about 35 mg of alendronate,

pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein the dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

5 30. A pharmaceutical composition suitable for oral administration for the treatment or prevention of abnormal bone resorption in mammals, in need thereof, comprising a unit dosage of a supplementary effective amount of at least about 2,800 IU of a non-activated metabolite of vitamin D₂ and/or D₃, and a
10 pharmaceutically effective amount of at least about 280 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein the dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

15 31. A pharmaceutical composition suitable for oral administration for the treatment or prevention of abnormal bone resorption in mammals, in need thereof, comprising a unit dosage of a supplementary effective amount of at least about 5,600 IU of a non-activated metabolite of vitamin D₂ and/or D₃, and a
20 pharmaceutically effective amount of at least about 280 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein the dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

25 32. A method of preventing or treating abnormal bone resorption in a mammal, in need thereof, comprising orally administering to said mammal a pharmaceutical composition comprising a unit dosage of a supplementary effective amount of at least about 2,800 IU of a non-activated metabolite of vitamin D₂ and/or D₃ and a pharmaceutically effective amount of at least about 280 mg of alendronate,
30 pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein the dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

33. A method of preventing or treating abnormal bone resorption in a mammal, in need thereof, comprising orally administering to said mammal a pharmaceutical composition comprising a unit dosage of a supplementary effective amount of at least about 5,600 IU of a non-activated metabolite of vitamin D₂ and/or D₃ and a pharmaceutically effective amount of at least about 35 mg of alendronate, pharmaceutically acceptable salts, derivatives, hydrates, and mixtures thereof, on an alendronic acid active weight basis, wherein the dosing interval is once-weekly, twice-weekly, bi-weekly, monthly, and bi-monthly.

10

34. The pharmaceutical composition according to Claim 27, wherein the abnormal bone resorption is selected from osteoporosis, osteopenia, Paget's disease, osteoarthritis, rheumatoid arthritis, metastatic bone disease, Gaucher's disease, avascular necrosis, polyostotic fibrous dysplasia, Charcot's joint, osteogenesis imperfecta, homocystinuria, lysinuric protein intolerance, Turner's syndrome, immobilization, fibrous dysplasia, fibrogenesis imperfecta ossium, periodontal disease, tooth loss, hypercalcemia of malignancy, and multiple myeloma.

15

35. The pharmaceutical composition according to Claim 34, wherein the form of the composition is selected from compressed tablets, coated tablets, un-coated tablets, capsules, hard capsules, gelatin capsules, pellets, elixirs, syrups, slurries, emulsions, suspensions, solutions, effervescent, buffered-effervescent, powders, and films.

20